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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,273	08/07/2002	Michel Perricaudet	ST99019 US PCT	8299

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
11/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/018,273	PERRICAUDET ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,13-15 and 17-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11,13-15 and 17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/2/2008 has been entered.

The amendment and the English translation of the foreign priority document filed 1/31/2008 and 9/2/2008 in response to the Office Action of 8/10/2007 are acknowledged and have been entered. Claims 1-5, 7-11, 13-15, and 17-32 are under examination.

It is noted that claim 16 has been canceled in the response of 5/21/2003. Applicant is reminded that full listing of claims including canceled claim 16 must be provided with the response to this Office Action.

Claim Rejections - 35 USC § 102

Rejection of claims 1-5, 7-9, 11, 13, 19, 22, 24, 26, 28, 30, and 31 under 35 U.S.C. 102(a) as being anticipated by Cho et al. (Gene Therapy, May 2000, Vol. 7, p. 740-749, Abstract in IDS of 6/30/2003) **is withdrawn** in view of Applicants submission of an English translation of the foreign priority document. All pending claims are given priority to June 11, 1999 and thus Cho et al. no longer constitutes prior art under 35 U.S.C. 102(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of claims 1-5, 7-9, 11, 13, 15, 17-19, 21, 22, 24, 26, 28, 30, and 31 under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224) **is maintained.**

Rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224) as applied to claims 1-5, and 7-9 and further in view of Sauvage (US Patent 6,022,708) **is maintained.**

Rejection of claims 14, 20, 23, 25, 27, 29 and 32 under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224) as applied to claims 1-5, 7-9, 11, 13, 15, 17-19, 21, 22, 24, 26, 28, 30, and 31 and further in view of Hidaka et al. (Thyroid, 1996, Vol. 6, p. 23-28) **is maintained.**

It is noted that all references cited in the rejections under 35 U.S.C. 103(a) above were publicly available prior to priority date of 6/11/1999. The submission of the foreign priority document does not overcome the rejections under 35 U.S.C. 103(a).

Response to Applicant's arguments

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that Applicants unexpectedly found the efficacy of expression of NIS (iodine transporter) in cancerous cells treated with an adenovirus harboring the NIS gene. Applicants argue that the relative uptake of ^{123}Iodine in Mandell's A375 tumor cells infected with retroviruses encoding NIS gene was ~7 fold greater than for non-transduced tumor cells, whereas in the present invention the level of ^{123}Iodine uptake was ~10 fold greater in tumor cells infected with adenoviral vectors encoding NIS compared to control tumor cells. Applicants argue that adenoviral vectors encoding NIS of the claimed invention unexpectedly display increased efficacy of radiolabeled iodine accumulation in the tumor cell compared to tumor cells transfected with Mandell's retroviral vectors encoding NIS.

In response to Applicants arguments the Office acknowledges that Example 4 in the present specification teaches ~10 fold greater ^{123}Iodine uptake in SiHa tumor cells infected with adenoviral vectors encoding NIS compared to control tumor cells; and that Mandell teaches ~7 fold greater uptake of ^{123}Iodine in A375 tumor cells infected with retroviruses encoding NIS gene compared to non-transduced tumor cells. It is the Office position that the experimental findings in Mandell and in present Example 4 cannot properly be compared to arrive at the conclusion of unexpected results, because Mandell and Example 4 use different cells. The Office notes that in addition to A375 human melanoma cells Mandell also teaches ^{123}Iodine uptake in IGROV human ovarian adenocarcinoma cells, CT26 mouse colon carcinoma cells, BNL.1 ME mouse transformed liver cells and FRTL-5 cell lines (see Results on page 663 and Figures 3 and 4). Mandell teaches 9 to 35 fold ^{123}Iodine uptake in FRTL-5 cells transduced with retroviral

vector encoding NIS gene (see page 633, right column, lines 3-14). As shown in Figure 4 of Mandell, the ^{123}Iodine uptake varies for each an every cell type transduced with the same retroviral vector encoding the NIS iodine transporter gene. Thus the cell type clearly affects the ^{123}Iodine uptake. The cells used in Example 4 of the present specification are SiHa human cervical carcinoma and represent yet another cell type. It is the Office's position that in order to arrive at a conclusion that the adenoviral vector expression of NIS gene is more efficacious than the retroviral vector expression of the NIS gene, the skilled artisan would have to compare the ^{123}Iodine uptake in one type of cells transduced with the adenoviral vector encoding the NIS gene and the retroviral vector encoding the NIS gene. Without such experimental testing the skilled artisan is unable to draw a conclusion that the adenoviral vector NIS gene expression is more efficacious than the retroviral NIS gene expression. Thus because the experimental results in Mandell and in Example 4 of the specification cannot accurately and properly be compared, Applicant's arguments of unexpected results are not convincing.

Applicants further argue that Mandell cannot properly be combined with Wilson, because the mechanism of replication for retrovirus and adenovirus are different and not interchangeable. Applicants argue that the skilled artisan would not have substituted Wilson's adenovirus for Mandell's retrovirus to express the iodine transporter gene, because there was no expectation of success. In response, the Examiner notes that different mechanisms of replication for retrovirus and adenovirus do not necessarily affect iodine transporter gene expression which is the objective of the present invention and thus the differences in replication mechanisms are irrelevant. As evidenced by Mandell the NIS gene is successfully expressed in the retroviral vector. Adenoviral heterologous gene expression has been successfully practiced in the art as

evidenced by Wilson, thus there would have been a reasonable expectation of success to express Mandell's iodine transporter in Wilson's adenoviral vector.

Applicant's arguments with regard to the references of Sauvage and Hidaka failing to remedy the deficiencies in Mandell and Wilson have been addressed in the Final Office Action of 8/10/2007.

The present invention would have been obvious to the skilled artisan as discussed above and on the record. Applicant's arguments fail to persuade and thus in view of the above the rejections are maintained.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday – Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Agnieszka Boesen/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648